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HBCU Summer Undergraduate Training Program in Prostate Cancer: A Partnership Between USU-CPDR and UDC

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14. ABSTRACT: Two meritorious students were selected under this Training Program in Prostate Cancer by USU-CPDR and UDC selection committee to provide motivating experience in the state-of-the-art CaP research. The main **objectives** were: **(a)** Recruit and motivate highly qualified undergraduate trainees from UDC, **(b)** expose UDC students to an intellectual environment that promotes state-of–the-art hands-on training and education in CaP research through special lectures by CPDR scientists and guest lectures, **(c)** motivate summer interns to contribute to CaP research centers at HBCUs, **(d)** to ensure that the new generation of biomedical scientists are properly trained to continue the fight against CaP. These objectives were achieved through the following Specific Aims: **Aim 1**. Selection of students and exposure to the state-of-the-art CaP research environment; **Aim 2**. Assignment of mentors and research project; **Aim 3**. Progress report preparation and presentation. **Results:** Two meritorious students were selected from a pool of applicants, to participate in this training program. Students were paired with mentors to work in an ongoing research projects. Prior to starting the research projects, the students were underwent Laboratory safety training and certified to work in the laboratory. Students were trained in basic techniques of cell biology, designing experiments, and conducting key experiments. Students presented their research goals and objectives and results obtained from their experiments in biweekly presentations. At the end of the training, each student made final presentation of the completed project. Each student was given a certificate of completion of achievement. **Conclusions:** The Students recruited under this collaborative research program were assigned to the faculty members of USUHS and given ongoing research projects covering of basic and translational aspects prostate cancer research to provide them with knowledge, expert guidance and tools to successfully complete the assignments. Research goals and objectives and experimental updates and progress were presented in biweekly presentations by all students. At the end of the training, each student presented the completed project and conclusions in a seminar and submitted the written project report to the supervisors. Each student was honored and recognized for their efforts and hard work with a certificate of completion of achievement. Overall, it was a very rewarding experience for the students as well as mentors.

15. SUBJECT TERMS: HBCU-Prostate Cancer Training, Center for Prostate Disease Research (CPDR), University of District of Columbia (UDC), DoD-PCRP, Uniformed Services University (USU), Department of Surgery, Walter Reed National Military Medical Center (WRNMMC), Basic Science Research Program (BSRP).

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HBCU Summer Undergraduate Training Program in Prostate Cancer Research

INTRODUCTION

The collaborative undergraduate student research program between the Uniformed Services University/Center for Prostate Disease Research (USU/CPDR) and the University of District of Columbia (UDC) was designed to train undergraduate students in prostate cancer research. The CPDR integrates a multidisciplinary approach to prostate cancer and continues to make great strides in clinical and basic sciences research for improving the entire spectrum of care including diagnosis, treatment, management, and follow-up for patients with the disease. CPDR has been in the forefront in major scientific breakthroughs and continue to identify and characterize new gene defects that have potential as new biomarkers and/or therapeutic targets for prostate cancer (CaP). In addition to the identification of alterations of the ETS related gene (ERG), CPDR scientists have been instrumental in identifying differences of major prostate cancer driver genes (*ERG and PTEN*) including discovery of a novel genomic alterations (e.g., *LSAMP)* that are enriched in African American prostate cancers. Our research goals are aligned with national priorities of reducing health disparity in African Americans through improving the understanding the biology of the disease in understudied patient populations. Embedded in our comprehensive prostate cancer translational research activities is the training of the next generation of physicians and scientists. The DoD-PCRP HBCU Summer Training Program at our Center continues to provide unique opportunities for highly motivated UDC college students to gain exposure to the state-of-the-art biomedical research in prostate cancer. Similar to the 1st and 2nd years of this grant reporting period, the collaborative team of USU-CPDR and UDC identified critical areas of prostate cancer research and developed well structured research projects for students of 3rd year focusing on molecular genetics and biological mechanisms of prostate cancer development and progression impacting prognosis and treatment; delineation of prognostic markers to distinguish indolent disease from aggressive prostate cancer; development of biomarkers to enhance prostate cancer diagnosis in African American patients. Students were trained by USU-CPDR faculty members with outstanding credentials in basic or clinical prostate cancer research. **The main objectives** of this training program were to: (1) recruit and motivate highly qualified undergraduate students from UDC; (2) expose the students to an intellectual environment, state-of –the art technologies and training and educating them in the advanced areas of CaP research; (3) motivate young researchers and cultivate interest in them to pursue prostate cancer research.

The following were the Specific Aims:

- **Selection of students and exposure to the state-of-the-art CaP research environment.** Meritorious students will be selected and exposed to a structured, well-rounded training program that integrates expertise, tools and motivation to pursue careers in prostate cancer research.
- **Assignment of mentors and research project.** The students will be paired with the mentors and will be assigned a specific short-term research project. Student will conduct experiments in their respective laboratories under the supervision of the mentors. During the 12 weeks period, the students will learn key issues in CaP research and will gain hands on experience in CaP molecular biology experiments.
- **Progress report preparation and presentation.** At the completion of training, the students will prepare a written report and present their research at institutional and national conferences.

HBCU Summer Undergraduate Training Program in Prostate Cancer: A Partnership between USU-CPDR and UDC is led by Dr. Shiv Srivastava, PhD, Principal Investigator/Program Director (USU-CPDR), Dr. Brandy Hudersen, PhD, Partnering PI (UDC) and Taduru Sreenath, PhD, Co-Investigator (USU-CPDR) in the management and administration of the award, selection of the students and mentors, pairing the students with the mentors, selection of the realistic and achievable projects, as well as the continued development and enhancement of this collaborative training program.

BODY

Task 1: Selection Process: To recruit the undergraduate students into the HBCU Summer Undergraduate Training Program in Prostate Cancer Research, the announcements were made at the UDC and on social media (Attachment # 1). The selection of the students was based on the transcripts and letters of recommendation and an essay of interest. This reporting period, 2 meritorious students were selected by USU-CPDR and UDC the selection committee composed of the faculty advisors for the summer Undergraduate Training Program, and PI and the Co-PI of the grant. The following were the successful applicants for the second year of the proposal:

- **Ms. Samerawat Desta** graduated in Associate in Science concentrated in Pre-Pharmacy at University of District of Columbia. Her future goal is to pursue higher studies in the Pharmaceutical sciences with an emphasis on the therapeutic aspects of cancers.

- **Mr. Randy Ricks** graduated from B.S. (Biology) University of the District of Columbia. Randy is proficient and familiar with bioinformatic resources such as NCBI, DbSNP, Entrez, Blast, Gene, and refSeq research. He received Stellar Researcher award from the University of the District of Columbia Cancer Research lab. His future goal is to enroll into medical school and to specialize in Oncology.

Task 2: Assignment of Mentors and Projects: Highly dedicated scientists from USU/CPDR with over 15-30 years of research experience, widely recognized in the clinical and basic science research in prostate cancer field served as mentors. All of these scientists have extensive experience in teaching and training urology residents from the Walter Reed National Military Medical Center and postdoctoral fellows and medical and undergraduate students from Uniformed Services University of the Health Sciences.

The projects carved out of ongoing CPDR research focus areas were selected on the basis of the research interests of the students. The goals for the students to carry out specific experiments in the research projects were set-up by the mentors with approval from the PIs. These projects were short-term realistic projects that provide the students with the knowledge, expert guidance and tools for successful completion.

Mentors:

The following are the Assignment of mentors, research projects:

Student:	Ms. Samerawat Desta Liberal Studies, Associate of Science (Pre-Pharmacy) University of District of Columbia, Washington DC
Mentors:	Dr. Ahmed Mohamed.
Project title:	Evaluation and characterization of ERG selective inhibitor, ERGi-USU and derivatives
Student:	Mr. Randy Ricks Major: Biology University of District of Columbia, Washington DC
Mentor:	Dr. Indu Kohaar, PhD.
Project title:	Association of TP53 Codon 72 Single-nucleotide Polymorphism (SNP) with Prostate Cancer

Task 3: Training, **Goals and Objectives:** The realistic goals and achievable objectives were designed for the students on the importance of understanding basic and translational aspects of prostate cancer research. During this training, students were educated on the current understanding of the main issues and challenges in the field of prostate cancer with an emphasis on the principles and practice of methods associated a specific research question and addressing them through a sound hypotheses, research design, methodologies, data collection, analysis, and data interpretations.

Student:	Ms. Samerawat Desta
Objectives:	To study the role of ribosomal biogenesis stress and identification of the mechanism of action of ERGi-USU in ERG positive tumor cells.
Student:	Mr. Randy Ricks
Objectives:	To perform association analysis of TP53 codon 72 SNP with clinico-pathological features (demographics, pathology and progression) of CaP.

Laboratory meetings: Through laboratory meetings, seminars and personal discussions the students interacted with other fellow students, faculty members and staff.

- **Weekly meetings:** Students participated in department seminars presented by the USU-CPDR faculty and researchers as well as guest speakers to understand the research activities and the progress in the field of prostate cancer.
- **Biweekly seminar presentations:** Students presented their goals and objectives and experimental plan for the training period in the first presentation and progress in subsequent presentations.

At the end of the summer experience, each student prepared and presented their research findings as PowerPoint presentations.

- **Final seminar presentation:** Students presented the complete project report, and conclusions.

- **Report Submission:** Each student submitted the entire project as a hard copy and an electronic version to the supervisors.

Task 4: Periodical meetings of Faculty advisors to monitor Student's progress: During the 12 weeks of the student training program, mentors interacted with students on a daily basis to review the results and design experimental plan for the day. Students and mentors met with Dr. Shiv Srivastava (PI/PD) and Dr. Taduru Sreenath (Co-Investigator) once a week to discuss the progress towards achieving goals and objectives of the project. Additionally, the students met with PI/PD and Co-Investigator for advises on specific academic goals and individual development plan (IDP). The monthly meetings were conducted to ensure periodic assessments of each student and assist the faculty mentors in determining appropriate interventions in order for the students to accomplish their goals and objectives.

Monitoring students' progress after the training period: PIs, Co-Investigators, faculty members and mentors continued to stay in touch through emails and on phone to monitor the to address any concerns towards their IDPs, selection of the study programs (graduate or professional), writing research statements and providing recommendation letters. The extended mentoring program will help in two important ways: (1) faculty mentoring for scientific exchanges and career advice, and (2) peer connection and peer mentoring where students will exchange their experiences and ideas with fellow students.

KEY RESEARCH ACCOMPLISHMENTS:

Students selected under the HBCU Summer Undergraduate Training Program in Prostate Cancer Research have successfully completed their projects assigned to them.

Highlights of their project outline and experimental results were the following:

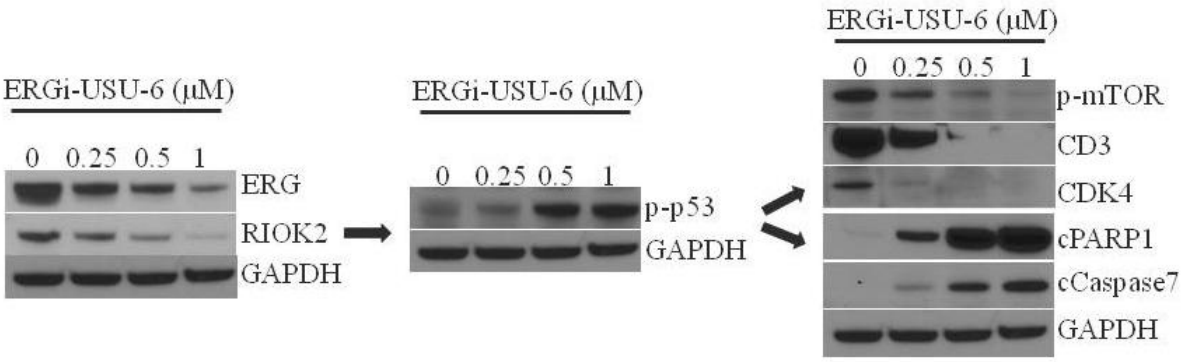
Student: Ms. Samerawat Desta
Mentors: Dr. Ahmed Mohamed, MD
Project title: Evaluation and characterization of ERG selective inhibitor, ERGi-USU and derivatives

Background: Prostate cancer is the most common diagnosed disease in men and Over 50% of prostate cancer cases show the presence of a TMPRSS2-ERG gene fusion on chromosome 21, which results in the oncogenic protein ERG. Oncogenic ERG proteins act as regulatory proteins that result in the proliferation of tumor cells. A small molecule inhibitor, ERGi-USU has been developed that has significantly inhibited ERG concentration in cancerous cells. In addition, ERGi-USU has proved to induce apoptosis in exposed cells.

Objectives: The main objective of the research project was to examining the role of ribosomal biogenesis stress and identification of the mechanism of action of ERGi-USU in ERG positive tumor cells.

Methods: Expression of ERG, mTOR, p53, PARP, Caspases and the proteins involved in the ribosomal biogenesis pathway such as RIOK2, RPps6, RPs6, RPs3, RPL7a, RPL13a along with GAPDH were analyzed by Western Blot assays in VCaP cell line treated with ERGi-USU and its derivatives.

Results: We observed dose dependent down regulation of RIOK2, ERG, mTOR, CD3 and CDK4 from 0.25 to 1 uM of ERGi-USU-6 treated VCaP cell extracts. However, the expression of phosphorylated p53, cleaved PARP1 and cleaved Caspase 7 were increased with the increasing concentrations of the ERGi-USU-6 treated VCaP cell extracts. Ribosomal biosynthesis proteins RPs3, and RPs6 were down regulated with the ERGi-USU-6 treatment.



Conclusion: ERGi-USU-6 follows the same pathway as the parental compound (ERGi-USU) by affecting ribosomal biogenesis and induced cell death through cell cycle arrest and apoptosis.
ERGi-USU showed inhibitory effect on RPs3 and RPs6 proteins but not significant as the RIOK2 and ERG. Inhibition of RIOK2, RPs3, and RPs6 was observed as early as 12 hour post treatment. RPL13a and RPL7a were minimally affected by the compound. These results suggest that the ERGi-USU and its derivative ERGi-USU-6 show increased cell death due to activation of apoptosis and inhibition of riobosomal biosynthesis pathways.

Student: Mr. Randy Ricks
Mentor: Dr. Indu Kohaar, PhD.
Project title: Association of TP53 Codon 72 Single-nucleotide Polymorphism (SNP) with Prostate Cancer

Background: Growing evidence indicates the involvement of a genetic component for prostate cancer (CaP) susceptibility. Quantitative estimates from twin studies have shown that about 42% of the variation in prostate cancer risk may be attributed to genetic components. Mutations in p53 have been associated with 50% of human cancers representing the most common somatic alteration in human cancers.

Objectives: To perform association analysis for *TP53* codon 72 single-nucleotide polymorphism (SNP) with clinico-pathological features of CaP.

Methods: Archived blood DNA samples from 923 patients, who underwent radical prostectomy, were obtained from CPDR bio specimen bank. Genomic DNA was extracted from blood using Qiagen Blood DNA extraction kit. Clinical characteristics including pathological, demographics and progression data were obtained from the CPDR database. TaqMan based SNP genotyping was performed using droplet digital polymerase chain reaction (ddPCR) approach. SNP genotype data was analyzed by QuantaSoft software (BioRad). Chi-square test was used to compare distributions of demographic and clinical pathologic characteristics across genotypes using SAS. All P-values were computed using two-sided statistical test with threshold set at 0.05.

Results: *TP53* codon 72C allele (Proline) is found to be the major allele in Caucasian-American (CA) patients and G allele (Arginine) is the major allele in African-American (AA) patients. The MAF distribution is found to be in concordance with publically available databases (1000G, HapMap). In CA patients, carriers of G allele (CG/GG) were found to be significantly associated with pathological T stage (p=0.027) and positive surgical margins (p=0.05). In AA patients, the carriers of G allele (CG/GG) were found to be associated with younger age of diagnosis (55.9yrs vs. 58.4yrs).

	CA				
	CC N=306 (54.84%)		CG+GG N=252 (45.16%)		p-value
	N	(%)	N	(%)	
Daignosed Age, Mean±SD	59.2 ± 0.4		60 ± 0.4		0.2646
Daignosed PSA, Mean±SD	5.9 ± 0.2		5.8 ± 0.3		0.7316
BCR	51	68.9	44	63.8	
Mets	8	66.7	8	66.7	
Clinic Gleason Sum					0.8889
Unknown/Missing	21	6.9	8	3.2	
<=6	203	66.3	178	70.6	
7	66	21.6	54	21.4	
8~10	16	5.2	12	4.8	
Clinic T Stage					0.1161
Unknown/Missing	7	2.3	8	3.2	
T1	178	58.2	156	61.9	
T2a~T2b	103	33.7	82	32.5	
>=T2c	18	5.9	6	2.4	
Pathologic T-Stage					**0.027**
Unknown/Missing	24	7.8	16	6.3	
T2	207	67.6	152	60.3	
T3~T4	75	24.5	84	33.3	
Pathologic Gleason Sum					0.2328
Unknown/Missing	13	4.2	6	2.4	
<=6	167	54.6	156	61.9	
7	95	31	72	28.6	
8~10	31	10.1	18	7.1	
Margin Status					**0.052**
Unknown/Missing	4	1.3	.	.	
Negative	247	80.7	189	75	
Positive	55	18	63	25	

	AA				
	GG N=107 (59%)		CG+CC N=154 (41%)		p-value
Daignosed Age, Mean±SD	N	(%)	N	(%)	
Daignosed PSA, Mean±SD	58.4± 0.8		55.9± 0.7		**0.0227**
BCR	6.4 ± 0.4		7.6 ± 0.9		0.6382
Mets	23	31.1	25	36.2	
Clinic Gleason Sum	4	33.3	4	33.3	
Unknown/Missing					0.5145
<=6	3	2.8	11	7.1	
7	67	62.6	102	66.2	
8~10	28	26.2	31	20.1	
Clinic T Stage	9	8.4	10	6.5	
Unknown/Missing					0.8645
T1	2	1.9	1	0.6	
T2a~T2b	77	72	111	72.1	
>=T2c	25	23.4	39	25.3	
Pathologic T-Stage	3	2.8	3	1.9	
Unknown/Missing					0.8745
T2	8	7.5	13	8.4	
T3~T4	76	71	107	69.5	
Pathologic Gleason Sum	23	21.5	34	22.1	
Unknown/Missing					0.2957
<=6	1	0.9	9	5.8	
7	53	49.5	86	55.8	
8~10	40	37.4	47	30.5	
Margin Status	13	12.1	12	7.8	
					0.9546
Unknown/Missing	2	1.9	4	2.6	
Negative	85	79.4	121	78.6	
Positive	20	18.7	29	18.8	

Conclusions: In conclusion, we examined the the association of TP53 Pro72Arg polymorphism and CaP in a case only study consisting of CA and AA patients. The present study clearly demonstrates population-dependent differences in allele frequencies of TP53 codon 72 SNP in AA and CA CaP, thereby providing a valuable framework for the interrogating CaP disparity among different ethnic groups. Additionally, we found a weak clinico-pathological association of the G allele (Arginine) in CA patients.

REPORTABLE OUTCOMES:

During this period, the students have displayed tremendous of interest in the field of prostate cancer and have gained experience.

- Oral presentations in the presence of faculty and staff of CPDR and senior leaderships of USU and UDC (Associate Dean/Chair of Math and Science, College of Arts and Sciences)
- Final reports of their research achievements were submitted to the mentors in a manuscript format
- Shared their research experiences, the knowledge they gained during this training period and expressed their interest in pursuing careers in medical and oncology research fields

CONCLUSIONS

This year, the student research training program was started with the meet and greet event to introduce students to the scientists and the other research staff. This was followed by the students meeting with Dr. Shiv Srivastava, Principal Investigator/Program Director, who provided them with an overview of the DoD-PCRP funded HBCU Summer Undergraduate Training Program in Prostate Cancer: A Partnership between USU-CPDR and UDC. The following were the activities of the students during the training period:

- Meet and greet event was organized to introduce the students to the CPDR staff
- Students' personal goals, objectives and their specific research interests were discussed
- HR related and personnel matters were discussed with the students in CPDR orientation meeting by Program Manager
- Laboratory safety training was given to the students by CPDR Laboratory Manager
- Short-term realistic projects within our ongoing **Basic and Translational research** were designed for students
- Mentors were assigned to the students by the PIs
- Discussions between mentor and student to identify a research project to include goals and objectives
- Students presentations to update their research progress to CPDR scientific staff and PI at CPDR Rockville location in biweekly meetings
- Students presented their complete project report and conclusions
- At the completion of training, the students prepared a complete written report to the mentors in a manuscript format

During this period, the students have displayed tremendous of interest in the field of prostate cancer and have gained experience. The results obtained from their experiments will be presented as posters in HBCU conferences at national level.

In summary, this collaborative training program has cultivated sufficient interest in students to understand the importance of prostate cancer research.

REFERENCES:

None

APPENDICES:

Supporting Data:

Summer Research Opportunity Announcement: **Attachment#1**

2017 SUMMER UNDERGRADUATE RESEARCH OPPORTUNITY

Summer research opportunity is available at the Department of Defense - Center for Prostate Disease Research (CPDR), Uniformed Services University (USU) *of Health Sciences* on a UDC-CPDR jointly funded program.

The Department of Defense, United States Army Medical Research and Materiel Command (USAMRMC), has awarded a new 3-year Prostate Cancer Research Program (PCRP) Collaborative Undergraduate Historically Black College And University Student Summer Training Program grant to the Uniformed Services University of the Health Sciences' (USU) Center for Prostate Disease Research (CPDR) and the University of the District of Columbia (UDC) collaborative team.

A successful collaborative effort between Dr. Deepak Kumar, from UDC and Dr. Shiv Srivastava, from USU/CPDR continues to provide a great opportunity for UDC students to take part in Prostate Cancer Training Program that is conducted during the summer break. The Program provides a 10-12 weeks summer research experience in prostate cancer research for undergraduates majoring in science, technology, engineering and mathematics (STEM) disciplines. The goal of this program is to prepare a diverse, highly talented, educated, and skilled pool of scientists interested in Prostate Cancer Research. The students will be exposed to cutting edge research methods in prostate cancer and will be mentored throughout their tenure at UDC. Several of past mentees are pursuing graduate and professional schools. More information about CPDR can be found at http://www.cpdr.org.

The Program has also been highlighted by the Department of Defense – CDMRP's Prostate Cancer Research Program. http://cdmrp.army.mil/pcrp/pbks/pcrppbk2014.pdf [page 13]

- **Four (4) students will be selected for summer, 2017 starting on June 1, 2017**

Eligibility Requirements

- The applicant must be a junior or senior at UDC when he/she returns to school in Fall 2017.
- Must be studying in STEM disciplines with an interest in Prostate Cancer Research.
- Must have a cumulative GPA of 3.0 or above at the time of application.

Stipend

- The participants to this program will receive a stipend @ $12/hr, 40h/week for 10-12 weeks.

Application

- Submit a letter of intent along with a short essay (1 page) on how this program will help you in achieving your career goals. The application must be submitted by email. The deadline for application is March 30, 2017. Selected applicants will be notified by April 30, 2017.

Submit your application to

Dr. Deepak Kumar
Co-PI and Director of the UDC-CPDR Summer Research Program
Division of Science and Mathematics
University of the District of Columbia
4200 Connecticut Avenue NW; Washington DC 20008
Email: dkumar@udc.edu